

A systematic review of the outcomes reported in trials of medication review in older patients: the need for a core outcome set

Running head: Outcomes reported in trials of medication review in older patients

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Summary

Aim: Medication review has been advocated as one of the measures to tackle the challenge of polypharmacy in older patients, yet there is no consensus on how best to evaluate its efficacy. This study aimed to assess outcome reporting in trials of medication review in older patients.

Methods: Randomized controlled trials (RCTs), prospective studies and RCT protocols involving medication review performed in patients aged 65 years or older in any setting of care were identified from: (1) a recent systematic review; (2) RCT registries of ongoing studies; (3) the Cochrane library. The type, definition, and frequency of all outcomes reported were extracted independently by two researchers.

Results: 47 RCTs or prospective published studies and 32 RCT protocols were identified. A total of 327 distinct outcomes were identified in the 47 published studies. Merely one fifth (21%) of the studies evaluated the impact of medication reviews on adverse events like adverse drug reactions or drug-related hospital admissions. Most of the outcomes were related to medication use (n=114, 35%) and healthcare use (n=74, 23%). Very few outcomes were patient related outcomes (n=24, 7%). A total of 248 distinct outcomes were identified in the 32 RCT protocols. Overall, the number of outcomes and the number and type of health domains covered by the outcomes varied largely.

Conclusion: Outcome reporting from RCTs concerning medication review in older patients is heterogeneous. This review highlights the need for a standardised core outcome set for medication review in older patients, to improve outcome reporting and evidence synthesis.

Introduction

Older patients are often exposed to polypharmacy [1,2]. This increases the risk of adverse drug reactions (ADR) and the cost of medications [3–6]. Performing a medication review has been shown to be an efficient approach to optimise the quality of prescriptions in older patients [7,8]. Medication review has been defined by the NICE guidelines as “a structured, critical examination of patient’s medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of medication related problems and reducing waste” [9].

Numerous randomized controlled trials (RCT) have been performed to evaluate the impact of medication review on clinical, patient reported, and economic outcomes. Several systematic reviews and meta-analyses have therefore been conducted to summarize the effectiveness of medication review in various settings [7,8,10–20]. However, the heterogeneity of outcomes reported in the RCTs has limited the quality of the conclusions of these systematic reviews. Robust meta-analyses could be performed for only a few outcomes, including hospitalisation and death [15–17,21]. For other outcomes, results were essentially summarized in a descriptive way because of heterogeneity in the choice and definition of the outcomes [17–20,22].

Outcome reporting bias is an under-recognised problem that affects the conclusions in a substantial proportion of systematic and Cochrane reviews [23–25]. This bias has been defined as selection (on the basis of the results) of a subset of the original variables recorded for inclusion in a study publication [26]. In a large unselected cohort of Cochrane systematic reviews, more than half of the reviews did not include full data for the review primary outcome of interest from all eligible trials [23]. Consequently, the updated Consolidated Standards of Reporting Trials (CONSORT) statement has recently recommended the use of identified and well defined outcomes in RCTs. In other fields of medicine, authors have conducted systematic reviews to reveal and quantify the heterogeneity and inconsistency of outcome reporting in a given research area [27–30]. According to the OMERACT

(Outcome Measures in Rheumatology) and the COMET (Core Outcome Measures in Effectiveness Trials) guidelines, some of these works have led to the development of core outcomes sets designed to increase the quality of outcome reporting and evidence synthesis in future research [31,32].

The purpose of this review was to undertake an in-depth analysis of outcome reporting to identify potential heterogeneity in outcomes reported from RCTs and prospective studies of medication review in older patients.

Methods

Study selection

We considered RCT, quasi-RCT, and other prospective interventional studies which investigated the effect of medication review performed in patients aged 65 years or older [33]. This age limit was widely used in trials of medication review during the last decades and corresponds to the WHO age limit to define older people. The following studies were excluded: studies published before 2000; studies predominantly including patients younger than 65 years old; retrospective studies; no outcome reported; sample size lower than 50 participants; medication reviews for a specific disease or condition (e.g. chronic heart failure) or as part of a multifaceted approach. By multifaceted approach we meant a complex intervention which contained additional interventions to the medication review (e.g. physiotherapy, nutritional advice, occupational therapy).

Search strategy

We performed a systematic review of published studies. Our starting point was the systematic review published in 2014 by Lehnbohm et al. [10], which purpose was to examine the evidence regarding the effectiveness of medication review to improve clinical outcomes. Lehnbohm et al. identified 43 studies published before March 2014 [10]. As the purpose of the present systematic review was different in nature, we only used the result of the search strategy, i.e. the list of the published studies included in the systematic review. Only the studies complying with our inclusion

and exclusion criteria were included. In addition, an update of the literature search using the same strategy/queries was performed for the period of March 2014 and July 2015 (the search strategy from [10] is given in supplementary data). Two reviewers (LP and JBB) independently assessed the title and abstracts of studies resulting from the searches. Full texts were investigated for all eligible published studies by two independent reviewers (LP and JBB). Any disagreement on the inclusion of a study was resolved by discussion and consensus. A third reviewer (AS) was involved if needed.

In addition, we used the search terms from the systematic review to identify RCTs protocols related to medication review on the following RCT websites: WHO international clinical trials registry platform: <http://apps.who.int/trialsearch/>; EU Clinical Trials Register:

<https://www.clinicaltrialsregister.eu/ctr-search/search>; US Clinical Trials register:

<https://clinicaltrials.gov>. Two independent reviewers (BB and JBB) first assessed the titles and

subsequently the summaries of the RCTs protocols identified by the queries. Any disagreement on

the inclusion of a study was resolved by discussion and consensus. A third reviewer (AS) was

involved if needed. It was verified if protocols had matured to full report publications. If this was the case, the paper was evaluated as mentioned above and added to the set of published studies.

Finally, the search terms from the systematic review were also used to identify relevant Cochrane reviews. A reviewer (JBB) identified the relevant Cochrane systematic reviews and then extracted the eligible original studies in the selected Cochrane systematic reviews. The selection process was checked by a second reviewer (AS).

Data extraction

An electronic data extraction form was developed with Epidata® software and pilot tested to increase the reliability of the data extractions. All data extractions on outcomes and outcome measurement instruments were performed by two independent reviewers (ST and JBB for RCT protocols; LP and JBB for published studies). Any disagreement was resolved by discussion and consensus. A third reviewer (AS) was involved if needed.

The characteristics of the RCT protocols and the published studies were extracted by one reviewer (JBB) and included: setting (hospital setting, primary care, nursing home); number of patients intended to be recruited (RCT protocols) or actually included (published studies); mean age (published studies only).

Outcomes used to compare the two groups under investigation (in RCTs and prospective before/after studies) or to evaluate the medication review process were extracted: name of the outcome in free text (what was measured in published studies and what was planned to be measured in protocols); primary or secondary outcome. For each outcome, the following data about measurement instrument were extracted from published studies: which instrument was used to measure the outcome (free text); was the method of measurement clearly defined (the reviewer answered “Yes” if he/she believed that another researcher could reproduce the procedure and its measurement with the explanations provided in the methods section). As the data provided in RCT protocols are often less detailed than in published studies, the data on measurement instrument were extracted when available.

Classification of outcomes into health domains and subdomains

The classification of the outcomes extracted from the included studies was achieved in several steps. Firstly, a list of 19 pre-defined subdomains corresponding to the most frequently reported outcomes (e.g. hospitalisation, all-cause death) were identified from the systematic review updated in this study [10]. These pre-defined subdomains were used by the two reviewers to associate each extracted outcome to a subdomain. The reviewers were free to propose a new subdomain if an outcome did not fit with the proposed subdomains. Secondly, a new list of subdomains was drafted on the basis of the pre-defined and the newly proposed subdomains. A consultation exercise was then performed with experts in clinical pharmacy and geriatricians. The objective was to get consensus on subdomain terms, to avoid major overlaps between subdomains, and to aggregate subdomains into health domains. The OMERACT filter 2.0 was used to organise this classification. A

total of 57 subdomains were identified and grouped into eight health domains (supplementary data; eTable 1).

Analysis

Quantitative variables were described by median, first and third quartiles (Q1, Q3), minimum and maximum because of skewed distributions. Qualitative variables were expressed as frequencies and percentages.

Results

Selection of studies and RCT protocols

In total, 47 published studies [34–80] and 32 RCT protocols were included in this systematic review. Details on the sources, reasons for exclusion, and selection process are presented in Figure 1.

Characteristics of the studies and RCT protocols included for data abstraction

The characteristics of the published studies and the RCT protocols included for data abstraction are provided in Table 1. The median number of participants included in published studies and intended to be included in RCTs described in protocols were similar. The studies were performed mainly in Europe, followed by Australia and USA. More recent RCT protocols have mainly been developed in European countries. The median number of outcomes per study or per RCT protocol was seven. This number varied importantly, from a single outcome in a published study [69] to 19 distinct outcomes in a RCT protocol [81].

Outcomes identified in the published studies and RCT protocols

The published studies and RCT protocols covered a median of four of the eight health domains identified (range: 1 to 6 for published studies; 2 to 7 for RCT protocols). The results are summarised in Figure 2 and detailed per sub-domains in eTable 2. More than 50% of all outcomes reported in published studies concerned medication use (e.g. the number of drugs, the number of potentially inappropriate medications, or overuse) or healthcare use (e.g. hospitalisations or GP visits). Other

health domains like patient reported outcomes, geriatric syndromes, or costs evaluation were far less frequently investigated. Only one fifth (21%) of the 47 published studies have evaluated the impact of medication reviews on adverse events such as ADR or drug-related hospital admissions. Consequently, less than one in ten published studies (n=4; 9%) had a primary outcome in the adverse event domain.

Outcomes related to medication use were reported by 89% of published studies and 94% of RCT protocols, suggesting an informal consensus on reporting this health domain. However, there was substantial variation in the subdomains used to explore this health domain between studies. Twelve different subdomains were identified and variously measured in the studies. The number of studies using each subdomains varied from only one time (“anticholinergic drug use” in 1 RCT protocols) to 26 times (“number of drugs” in 17 published studies and 9 RCT protocols). Eight of these 12 subdomains were used at least once as a primary outcome in a published study or in a RCT protocol.

This between-subdomain heterogeneity was also observed for the seven other health domains, as detailed in eTable 2. For example, seven, 10, and 12 different subdomains were variously used to explore the healthcare use, patient-reported outcome, and geriatric syndromes domains, respectively. In total, nearly half of the subdomains (n=28; 49%) were used by less than 10% of the 79 selected studies (published studies and RCT protocols). Conversely, only four subdomains were used by a third or more of the 79 selected studies, namely “number of drugs”, “hospitalisation”, “all-cause death”, and “health-related quality of life”.

Clarity of measurement instrument reported

The total number of outcomes and the specific number of outcomes for which an instrument measurement was clearly described in the methods are presented per health domain in Table 2 and per subdomain in supplementary data (eTable 3). In total, the measurement instruments were considered clearly reported in 52% to 83% of all domains, except for cost outcomes. In the costs domain, the methods most often insufficiently described the source of drug costs or costs related to

healthcare use, or the way in which calculations were performed. For medication use, the methods were considered clear in two thirds (65%) of the outcomes. The outcomes most often considered poorly defined were the outcomes “Number of drugs”, and “Drug-drug interactions”.

Discussion

This systematic review provides an analysis on which health domains have been and are currently evaluated in published and planned/ongoing studies (RCT protocols) of medication review in older patients. It reveals that there is substantial heterogeneity, as the number of outcomes and the number and type of health domains covered by the outcomes vary from one study to another. Furthermore, it shows that some essential health domains including adverse events and patient related outcomes have been poorly evaluated in published studies. These results highlight the need for developing a core outcome set for medication review in older patients. Having strong outcome data would help clarifying if and how medication review can be effective, among which population, in which context, and what are the important contextual factors which support positive outcomes.

Not surprisingly, our results have shown that most studies of medication review in older patients have reported, or planned to report, outcomes related to the medication use domain. These outcomes were often the primary outcomes. However, the 13 distinct subdomains identified in the medication use domain were variously used by authors (eTable2). Despite this heterogeneity between subdomains, several systematic reviews of RCTs have tried to summarize the effect of medication review on such outcomes. Their results showed that medication review is effective in improving drug appropriateness, drug underuse, or potentially inappropriate prescribing, but there were more conflicting results for drug-related problems [7,8,18,20]. Evaluating the effects of medication review on more specific outcomes such as inappropriate use of antipsychotic drugs was limited due to inconsistency in the various definitions of the outcome used across the studies [22]. We identified that clarity in the reporting of the measurement instruments in some domains varied

substantially and this impacts upon the extent to which the outcomes from such studies can be accurately interpreted, and may limit the validity of comparison of results across studies.

Our results also show that many published studies have reported outcomes related to the use of healthcare resources domain, mainly hospitalisations. Meta-analyses however have failed to identify a significant effect of medication review on hospital admissions, length of hospital stays, or emergency department visits [12,15–17,21,82]. These negative results may have discouraged new studies to use this outcomes as a primary outcome. One hypothesis is that these outcomes are influenced by many other factors, which could explain why this outcome is less often used as primary outcome in RCT protocols.

Ten (21%) published studies reported outcomes related to the adverse events domain. This may be due to the difficulty in detecting and adjudicating adverse events prospectively during an RCT.

Hence, the effects of medication review on ADR or drug-related hospital admissions remain unclear and have not been assessed by any meta-analysis. Reporting bias of harm outcomes in RCTs and systematic reviews has been identified as an important problem [83]. It seems particularly detrimental that harm outcomes have been so poorly reported in RCTs of medication review, as the purpose of this intervention is actually to manage the risk of prescribed drugs and to reduce the number of drug-related problems. A higher proportion of on-going studies planned to report adverse events according to their protocols. However, it is uncertain whether this greater focus on these outcomes in protocols will be released in the final studies' results. Outcomes related to costs were also less extensively investigated. The effect of medication review on costs is therefore most often analysed through a narrative approach in systematic reviews [13,20].

Patient reported outcomes have been investigated in 43% of published studies and are planned to be investigated in 69% of RCT protocols. Most of these outcomes concern health-related quality of life (eTable 2). Very few studies have investigated or will investigate subdomains like drug-regimen complexity or the alignment of drug regimen with patient preference, although these aspects are included in the definition of a medication review [9].

Several systematic reviews of medication review identified that inconsistency and imprecision in outcome reporting limited their analyses and conclusions [13,14,17,18,20,22]. Our present review has confirmed and extended these findings. While other systematic reviews aimed at pooling and summarizing results on a limited number of outcomes, we have extracted and reported all kinds of outcomes used in this field. Several authors have used hospitalisation or mortality to assess the clinical effectiveness of a medication review [12,15,16,21]. However, our results suggest that the choice to perform meta-analyses on these outcomes are most likely related to the high proportion of studies reporting these outcomes as opposed to their relevance. In fact, hospitalisation or death in older patients with polypharmacy and multimorbidity can be related to many factors other than medications [84,85]. Incidence of ADR or drug-related hospital admissions may be more relevant to assess the effectiveness of a medication review, but it is indeed much more difficult and time-consuming to detect and adjudicate properly all ADEs or drug-related hospital admissions during a RCT than to record all-causes hospitalisations or mortality.

In summary, our results highlight the need for a core outcome set (COS) for future studies of medication review in older patients. A COS is an agreed standardised collection of outcome variables which should be measured and reported in all trials for a specific condition or clinical area. The development of a COS would tackle the challenge of obtaining a consensus on which outcomes are deemed essential for all stakeholders involved in the management of a given condition, including patients. It has the potential to reduce heterogeneity between trials, lead to research that is more likely to measure relevant outcomes, and enhance the value of evidence synthesis by reducing the risk of outcome reporting bias and ensure that all trials report usable information [86–88].

Moreover, in a second step, the measurement instrument recommended to be used to evaluate each outcome included in the COS can be determined [89]. This aspect may be important as our study has shown that the methods were not clearly detailed in a significant proportion of studies for all categories of domains and subdomains. A consensus on the measurement instrument has also the potential to increase the quality of value of evidence from subsequent systematic reviews and allowing meaningful meta-analyses to be performed. As part of the European Commission-funded OPERAM project, this systematic review will serve as a starting point to developing a COS for clinical trials of medication review in older patients. The OPERAM project will perform a multicentre randomised controlled trial to assess the impact of an intervention to optimise pharmacotherapy and to enhance compliance in 1900 multimorbid patients aged 70 years and older. In order to tackle the challenge of measuring relevant outcomes for these patients, the OPERAM project included the development a COS suitable for all settings.

Some limitations of this review should be mentioned. As the aim of this project was of descriptive nature, we did not perform analytical analyses to formally compare results from published studies and protocol, and had a too low number of studies to evaluate if the between study variation could be partially explained by the setting (hospitalised versus nursery home versus community dwelling). This systematic review stopped in July 2015, more than one year before its submission. However, the variation in outcome reporting between published studies should not have changed considerably and has been captured indirectly through the analysis of RCT protocols. It seems therefore unlikely that an updated version would have impacted on the results. The selection criteria were those from the initial systematic review by Lehnborn et al. [10], which could have influenced the outcomes identified. For example, smaller studies with less than 50 subjects, which were excluded from the review, may have reported outcomes that require detailed review of patients or records, such as ADRs or drug-related admissions, more often. Variation between studies was investigated descriptively at the subdomain level but we didn't report variation between outcomes in a given subdomain. The outcomes may vary in a subdomain in the way they were reported (e.g. number of

potentially inappropriate medications per patient or number of patients with at least one potentially inappropriate medication) or in the way they were measured (e.g. Beers criteria, STOPP criteria, PRISCUS list). Another limitation is that the categorization into domains and subdomains may be somehow arbitrary. We were also reliant upon the descriptions of domains and measures in the published studies and, as we identified, at times these were not clearly described. We used a consultation exercise as other studies or study protocols have [30,90], as we could not identify an existing framework to guide this process.

Conclusion

This systematic review revealed a significant heterogeneity in outcome reporting in studies of medication review in older patients. Some essential health areas including adverse events and patient reported outcomes have been insufficiently evaluated. We advocate the development of a COS to improve the quality of outcome reporting and evidence synthesis in future research in this important field.

Competing interest

All authors have completed the Unified Competing Interest form and declare no support from any organization for the submitted work.

Authors contribution

JBB conceptualized and designed the study, performed the selection of studies and data extraction, carried out analyses and interpretation of data, drafted the initial manuscript, and approved the final manuscript as submitted.

LGP designed the study, performed the selection of studies and data extraction, critically reviewed the manuscript and approved the final manuscript as submitted.

ST performed data extraction, critically reviewed the manuscript and approved the final manuscript as submitted.

BB performed the selection of studies, critically reviewed the manuscript and approved the final manuscript as submitted.

OD participated in study design and critically reviewed the manuscript and approved the final manuscript as submitted.

AR participated in study design and critically reviewed the manuscript and approved the final manuscript as submitted.

JW designed the study, critically reviewed the manuscript and approved the final manuscript as submitted.

AS conceptualized and designed the study, checked the selection of studies and data extraction, carried out interpretation of data, drafted the initial manuscript, and approved the final manuscript as submitted.

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References

- [1] Payne RA, Avery AJ, Duerden M, Saunders CL, Simpson CR, Abel GA. Prevalence of polypharmacy in a Scottish primary care population. *Eur J Clin Pharmacol* 2014; 70:575–581.
- [2] Hovstadius B, Hovstadius K, Astrand B, Petersson G. Increasing polypharmacy - an individual-based study of the Swedish population 2005-2008. *BMC Clin Pharmacol* 2010; 10:16.
- [3] Pirmohamed M, James S, Meakin S, Green C, Scott AK, Walley TJ, Farrar K, Park BK, Breckenridge AM. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ* 2004; 329:15–19.
- [4] Ma J, Wang Y, Gao M, Meng Q, Liu J. Adverse drug reactions as the cause of emergency department admission of patients aged 80 years and older. *Eur J Intern Med* 2012; 23:e162–e163.
- [5] Conforti A, Costantini D, Zanetti F, Moretti U, Grezzana M, Leone R. Adverse drug reactions in older patients: an Italian observational prospective hospital study. *Drug Healthc Patient Saf* 2012; 4:75–80.
- [6] Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. *Ann Pharmacother* 2008; 42:1017–1025.
- [7] Patterson SM, Cadogan CA, Kerse N, Cardwell CR, Bradley MC, Ryan C, Hughes C. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 2014.
- [8] Meid AD, Lampert A, Burnett A, Seidling HM, Haefeli WE. The impact of pharmaceutical care interventions for medication underuse in older people: a systematic review and meta-analysis. *Br J Clin Pharmacol* 2015.
- [9] Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes | Guidance and guidelines | NICE. <https://www.nice.org.uk/guidance/ng5>. Accessed 31 May 2016.
- [10] Lehnbohm EC, Stewart MJ, Manias E, Westbrook JL. Impact of Medication Reconciliation and Review on Clinical Outcomes. *Ann Pharmacother* 2014; 48:1298–1312.
- [11] Hatah E, Braund R, Tordoff J, Duffull SB. A systematic review and meta-analysis of pharmacist-led fee-for-services medication review. *Br J Clin Pharmacol* 2014; 77:102–115.
- [12] Christensen M, Lundh A. Medication review in hospitalised patients to reduce morbidity and mortality. *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd; 1996.
- [13] Graabæk T, Kjeldsen LJ. Medication Reviews by Clinical Pharmacists at Hospitals Lead to Improved Patient Outcomes: A Systematic Review. *Basic Clin Pharmacol Toxicol* 2013; 112:359–373.
- [14] Forsetlund L, Eike MC, Gjerberg E, Vist GE. Effect of interventions to reduce potentially inappropriate use of drugs in nursing homes: a systematic review of randomised controlled trials. *BMC Geriatr* 2011; 11:16.
- [15] Wallerstedt SM, Kindblom JM, Nylén K, Samuelsson O, Strandell A. Medication reviews for nursing home residents to reduce mortality and hospitalization: systematic review and meta-analysis. *Br J Clin Pharmacol* 2014; 78:488–497.
- [16] Thomas R, Huntley AL, Mann M, Huws D, Elwyn G, Paranjothy S, Purdy S. Pharmacist-led interventions to reduce unplanned admissions for older people: a systematic review and meta-analysis of randomised controlled trials. *Age Ageing* 2014; 43:174–187.
- [17] Holland R, Desborough J, Goodyer L, Hall S, Wright D, Loke YK. Does pharmacist-led medication review help to reduce hospital admissions and deaths in older people? A systematic review and meta-analysis. *Br J Clin Pharmacol* 2008; 65:303–316.

- [18] Alldred DP, Kennedy M-C, Hughes C, Chen TF, Miller P. Interventions to optimise prescribing for older people in care homes. Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd; 2016.
- [19] Geurts MME, Talsma J, Brouwers JRB, de Gier JJ. Medication review and reconciliation with cooperation between pharmacist and general practitioner and the benefit for the patient: a systematic review. *Br J Clin Pharmacol* 2012; 74:16–33.
- [20] Viswanathan M, Kahwati LC, Golin CE, Blalock SJ, Coker-Schwimmer E, Posey R, Lohr KN. Medication therapy management interventions in outpatient settings: a systematic review and meta-analysis. *JAMA Intern Med* 2015; 175:76–87.
- [21] Hohl CM, Wickham ME, Sobolev B, Perry JJ, Sivilotti MLA, Garrison S, Lang E, Brasher P, Doyle-Waters MM, Brar B, Rowe BH, Lexchin J, et al. The effect of early in-hospital medication review on health outcomes: a systematic review. *Br J Clin Pharmacol* 2015.
- [22] Thompson Coon J, Abbott R, Rogers M, Whear R, Pearson S, Lang I, Cartmell N, Stein K. Interventions to reduce inappropriate prescribing of antipsychotic medications in people with dementia resident in care homes: a systematic review. *J Am Med Dir Assoc* 2014; 15:706–718.
- [23] Kirkham JJ, Dwan KM, Altman DG, Gamble C, Dodd S, Smyth R, Williamson PR. The impact of outcome reporting bias in randomised controlled trials on a cohort of systematic reviews. *BMJ* 2010; 340:c365.
- [24] Hart B, Lundh A, Bero L. Effect of reporting bias on meta-analyses of drug trials: reanalysis of meta-analyses. *BMJ* 2012; 344:d7202.
- [25] Page MJ, McKenzie JE, Kirkham J, Dwan K, Kramer S, Green S, Forbes A. Bias due to selective inclusion and reporting of outcomes and analyses in systematic reviews of randomised trials of healthcare interventions. *Cochrane Database Syst Rev* 2014; 10:MR000035.
- [26] Hutton JL, Williamson PR. Bias in meta-analysis due to outcome variable selection within studies. *J R Stat Soc Ser C Appl Stat* 2000; 49:359–370.
- [27] Wylde V, Bruce J, Beswick A, Elvers K, Gooberman-Hill R. Assessment of chronic postsurgical pain after knee replacement: a systematic review. *Arthritis Care Res* 2013; 65:1795–1803.
- [28] Potter S, Brigic A, Whiting PF, Cawthorn SJ, Avery KNL, Donovan JL, Blazeby JM. Reporting clinical outcomes of breast reconstruction: a systematic review. *J Natl Cancer Inst* 2011; 103:31–46.
- [29] Rodgers S, Brealey S, Jefferson L, McDaid C, Maund E, Hanchard N, Goodchild L, Spencer S. Exploring the outcomes in studies of primary frozen shoulder: is there a need for a core outcome set? *Qual Life Res Int J Qual Life Asp Treat Care Rehabil* 2014; 23:2495–2504.
- [30] Hopkins JC, Howes N, Chalmers K, Savovic J, Whale K, Coulman KD, Welbourn R, Whistance RN, Andrews RC, Byrne JP, Mahon D, Blazeby JM. Outcome reporting in bariatric surgery: an in-depth analysis to inform the development of a core outcome set, the BARIACT Study. *Obes Rev Off J Int Assoc Study Obes* 2015; 16:88–106.
- [31] Wylde V, MacKichan F, Bruce J, Gooberman-Hill R. Assessment of chronic post-surgical pain after knee replacement: development of a core outcome set. *Eur J Pain Lond Engl* 2015; 19:611–620.
- [32] Potter S, Holcombe C, Ward JA, Blazeby JM, BRAVO Steering Group. Development of a core outcome set for research and audit studies in reconstructive breast surgery. *Br J Surg* 2015; 102:1360–1371.
- [33] Higgins J, Green S. Cochrane Handbook for Systematic Reviews of Interventions. vol. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration. 2011.
- [34] Gillespie U, Alassaad A, Henrohn D, Garmo H, Hammarlund-Udenaes M, Toss H, Kettis-Lindblad A, Melhus H, Mörlin C. A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. *Arch Intern Med* 2009; 169:894–900.
- [35] Mortimer C, Emmerton L, Lum E. The impact of an aged care pharmacist in a department of emergency medicine. *J Eval Clin Pract* 2011; 17:478–485.

- [36] Spinewine A, Swine C, Dhillon S, Lambert P, Nachega JB, Wilmotte L, Tulkens PM. Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial. *J Am Geriatr Soc* 2007; 55:658–665.
- [37] Lisby M, Thomsen A, Nielsen LP, Lyhne NM, Breum-Leer C, Fredberg U, Jørgensen H, Brock B. The effect of systematic medication review in elderly patients admitted to an acute ward of internal medicine. *Basic Clin Pharmacol Toxicol* 2010; 106:422–427.
- [38] Hellström LM, Bondesson A, Höglund P, Midlöv P, Holmdahl L, Rickhag E, Eriksson T. Impact of the Lund Integrated Medicines Management (LIMM) model on medication appropriateness and drug-related hospital revisits. *Eur J Clin Pharmacol* 2011; 67:741–752.
- [39] Browne C, Kingston C, Keane C. Falls prevention focused medication review by a pharmacist in an acute hospital: implications for future practice. *Int J Clin Pharm* 2014; 36:969–975.
- [40] Bergqvist M, Ulfvarson J, Karlsson EA. Nurse-led medication reviews and the quality of drug treatment of elderly hospitalized patients. *Eur J Clin Pharmacol* 2009; 65:1089–1096.
- [41] Schmader KE, Hanlon JT, Pieper CF, Sloane R, Ruby CM, Twersky J, Francis SD, Branch LG, Lindblad CI, Artz M, Weinberger M, Feussner JR, et al. Effects of geriatric evaluation and management on adverse drug reactions and suboptimal prescribing in the frail elderly. *Am J Med* 2004; 116:394–401.
- [42] Gallagher P, O'Connor M, O'Mahony D. Prevention of Potentially Inappropriate Prescribing for Elderly Patients: A Randomized Controlled Trial Using STOPP/START Criteria. *Clin Pharmacol Ther* 2011; 89:845–854.
- [43] Krska J, Cromarty JA, Arris F, Jamieson D, Hansford D, Duffus PR, Downie G, Seymour DG. Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. *Age Ageing* 2001; 30:205–211.
- [44] Nazareth I, Burton A, Shulman S, Smith P, Haines A, Timberval H. A pharmacy discharge plan for hospitalized elderly patients--a randomized controlled trial. *Age Ageing* 2001; 30:33–40.
- [45] Zermansky AG, Petty DR, Raynor DK, Freemantle N, Vail A, Lowe CJ. Randomised controlled trial of clinical medication review by a pharmacist of elderly patients receiving repeat prescriptions in general practice. *BMJ* 2001; 323:1340–1343.
- [46] Sellors J, Kaczorowski J, Sellors C, Dolovich L, Woodward C, Willan A, Goeree R, Cosby R, Trim K, Sebaldt R, Howard M, Hardcastle L, et al. A randomized controlled trial of a pharmacist consultation program for family physicians and their elderly patients. *CMAJ Can Med Assoc J J Assoc Medicale Can* 2003; 169:17–22.
- [47] Naunton M, Peterson GM. Evaluation of Home-Based Follow-Up of High-Risk Elderly Patients Discharged from Hospital. *J Pharm Pract Res* 2003; 33:176–182.
- [48] Sturgess IK, McElnay JC, Hughes CM, Crealey G. Community pharmacy based provision of pharmaceutical care to older patients. *Pharm World Sci PWS* 2003; 25:218–226.
- [49] Holland R, Lenaghan E, Harvey I, Smith R, Shepstone L, Lipp A, Christou M, Evans D, Hand C. Does home based medication review keep older people out of hospital? The HOMER randomised controlled trial. *BMJ* 2005; 330:293.
- [50] Lenaghan E, Holland R, Brooks A. Home-based medication review in a high risk elderly population in primary care--the POLYMED randomised controlled trial. *Age Ageing* 2007; 36:292–297.
- [51] Fiss T, Dreier A, Meinke C, van den Berg N, Ritter CA, Hoffmann W. Frequency of inappropriate drugs in primary care: analysis of a sample of immobile patients who received periodic home visits. *Age Ageing* 2011; 40:66–73.
- [52] Bryant LJM, Coster G, Gamble GD, McCormick RN. The General Practitioner-Pharmacist Collaboration (GPPC) study: a randomised controlled trial of clinical medication reviews in community pharmacy. *Int J Pharm Pract* 2011; 19:94–105.
- [53] Elliott RA, Martinac G, Campbell S, Thorn J, Woodward MC. Pharmacist-led medication review to identify medication-related problems in older people referred to an Aged Care Assessment Team: a randomized comparative study. *Drugs Aging* 2012; 29:593–605.

- [54] Furniss L, Burns A, Craig SK, Scobie S, Cooke J, Faragher B. Effects of a pharmacist's medication review in nursing homes. Randomised controlled trial. *Br J Psychiatry J Ment Sci* 2000; 176:563–567.
- [55] Roberts MS, Stokes JA, King MA, Lynne TA, Purdie DM, Glasziou PP, Wilson DA, McCarthy ST, Brooks GE, de Looze FJ, Del Mar CB. Outcomes of a randomized controlled trial of a clinical pharmacy intervention in 52 nursing homes. *Br J Clin Pharmacol* 2001; 51:257–265.
- [56] King MA, Roberts MS. Multidisciplinary case conference reviews: improving outcomes for nursing home residents, carers and health professionals. *Pharm World Sci PWS* 2001; 23:41–45.
- [57] Crotty M, Halbert J, Rowett D, Giles L, Birks R, Williams H, Whitehead C. An outreach geriatric medication advisory service in residential aged care: a randomised controlled trial of case conferencing. *Age Ageing* 2004; 33:612–617.
- [58] Zermansky AG, Alldred DP, Petty DR, Raynor DK, Freemantle N, Eastaugh J, Bowie P. Clinical medication review by a pharmacist of elderly people living in care homes--randomised controlled trial. *Age Ageing* 2006; 35:586–591.
- [59] Patterson SM, Hughes CM, Crealey G, Cardwell C, Lapane KL. An evaluation of an adapted U.S. model of pharmaceutical care to improve psychoactive prescribing for nursing home residents in northern ireland (fleetwood northern ireland study). *J Am Geriatr Soc* 2010; 58:44–53.
- [60] Pope G, Wall N, Peters CM, O'Connor M, Saunders J, O'Sullivan C, Donnelly TM, Walsh T, Jackson S, Lyons D, Clinch D. Specialist medication review does not benefit short-term outcomes and net costs in continuing-care patients. *Age Ageing* 2011; 40:307–312.
- [61] Lapane KL, Hughes CM, Daiello LA, Cameron KA, Feinberg J. Effect of a pharmacist-led multicomponent intervention focusing on the medication monitoring phase to prevent potential adverse drug events in nursing homes. *J Am Geriatr Soc* 2011; 59:1238–1245.
- [62] Milos V, Rekman E, Bondesson Å, Eriksson T, Jakobsson U, Westerlund T, Midlöv P. Improving the quality of pharmacotherapy in elderly primary care patients through medication reviews: a randomised controlled study. *Drugs Aging* 2013; 30:235–246.
- [63] Blalock SJ, Casteel C, Roth MT, Ferreri S, Demby KB, Shankar V. Impact of enhanced pharmacologic care on the prevention of falls: a randomized controlled trial. *Am J Geriatr Pharmacother* 2010; 8:428–440.
- [64] Meredith S, Feldman P, Frey D, Giammarco L, Hall K, Arnold K, Brown NJ, Ray WA. Improving medication use in newly admitted home healthcare patients: a randomized controlled trial. *J Am Geriatr Soc* 2002; 50:1484–1491.
- [65] Dalleur O, Boland B, Losseau C, Henrard S, Wouters D, Speybroeck N, Degryse JM, Spinewine A. Reduction of potentially inappropriate medications using the STOPP criteria in frail older inpatients: a randomised controlled study. *Drugs Aging* 2014; 31:291–298.
- [66] Trygstad TK, Christensen D, Garmise J, Sullivan R, Wegner S. Pharmacist response to alerts generated from Medicaid pharmacy claims in a long-term care setting: results from the North Carolina polypharmacy initiative. *J Manag Care Pharm JMCP* 2005; 11:575–583.
- [67] Pit SW, Byles JE, Henry DA, Holt L, Hansen V, Bowman DA. A Quality Use of Medicines program for general practitioners and older people: a cluster randomised controlled trial. *Med J Aust* 2007; 187:23–30.
- [68] Kwint HF, Faber A, Gussekloo J, Bouvy ML. Effects of medication review on drug-related problems in patients using automated drug-dispensing systems: a pragmatic randomized controlled study. *Drugs Aging* 2011; 28:305–314.
- [69] Gnjjidic D, Le Couteur DG, Abernethy DR, Hilmer SN. A Pilot Randomized Clinical Trial Utilizing the Drug Burden Index to Reduce Exposure to Anticholinergic and Sedative Medications in Older People. *Ann Pharmacother* 2010; 44:1725–1732.
- [70] Touchette DR, Masica AL, Dolor RJ, Schumock GT, Choi YK, Kim Y, Smith SR. Safety-focused medication therapy management: a randomized controlled trial. *J Am Pharm Assoc JAPhA* 2012; 52:603–612.

- [71] Frankenthal D, Lerman Y, Kalendariev E, Lerman Y. Intervention with the Screening Tool of Older Persons Potentially Inappropriate Prescriptions/Screening Tool to Alert Doctors to Right Treatment Criteria in Elderly Residents of a Chronic Geriatric Facility: A Randomized Clinical Trial. *J Am Geriatr Soc* 2014; 62:1658–1665.
- [72] Ahmad A, Nijpels G, Dekker JM, Kostense PJ, Hugtenburg JG. Effect of a pharmacist medication review in elderly patients discharged from the hospital. *Arch Intern Med* 2012; 172:1346–1347.
- [73] Lisby M, Bonnerup DK, Brock B, Gregersen PA, Jensen J, Larsen M-L, Rungby J, Sonne J, Mainz J, Nielsen LP. Medication Review and Patient Outcomes in an Orthopedic Department: A Randomized Controlled Study. *J Patient Saf* 2015.
- [74] Chan D-C, Chen J-H, Wen C-J, Chiu L-S, Wu S-C. Effectiveness of the medication safety review clinics for older adults prescribed multiple medications. *J Formos Med Assoc Taiwan Yi Zhi* 2014; 113:106–113.
- [75] Jódar-Sánchez F, Malet-Larrea A, Martín JJ, García-Mochón L, López Del Amo MP, Martínez-Martínez F, Gastelurrutia-Garralda MA, García-Cárdenas V, Sabater-Hernández D, Sáez-Benito L, Benrimoj SI. Cost-utility analysis of a medication review with follow-up service for older adults with polypharmacy in community pharmacies in Spain: the conSIGUE program. *PharmacoEconomics* 2015; 33:599–610.
- [76] Lenander C, Elfsson B, Danielsson B, Midlöv P, Hasselström J. Effects of a pharmacist-led structured medication review in primary care on drug-related problems and hospital admission rates: a randomized controlled trial. *Scand J Prim Health Care* 2014; 32:180–186.
- [77] Mestres C, Hernandez M, Llagostera B, Espier M, Chandre M. Improvement of pharmacological treatments in nursing homes: medication review by consultant pharmacists. *Eur J Hosp Pharm* 2015:ejhpharm-2014-000508.
- [78] O'Sullivan D, O'Mahony D, O'Connor MN, Gallagher P, Cullinan S, O'Sullivan R, Gallagher J, Eustace J, Byrne S. The impact of a structured pharmacist intervention on the appropriateness of prescribing in older hospitalized patients. *Drugs Aging* 2014; 31:471–481.
- [79] Paquin AM, Salow M, Rudolph JL. Pharmacist calls to older adults with cognitive difficulties after discharge in a Tertiary Veterans Administration Medical Center: a quality improvement program. *J Am Geriatr Soc* 2015; 63:571–577.
- [80] Westberg SM, Swanoski MT, Renier CM, Gessert CE. Evaluation of the impact of comprehensive medication management services delivered posthospitalization on readmissions and emergency department visits. *J Manag Care Spec Pharm* 2014; 20:886–893.
- [81] Cooperation for Improved Pharmacotherapy in Home-dwelling Elderly People Receiving Polypharmacy - The COOP Study - Tabular View - ClinicalTrials.gov. <https://clinicaltrials.gov/ct2/show/record/NCT02379455>. Accessed 10 August 2016.
- [82] Page AT, Clifford RM, Potter K, Schwartz D, Etherton-Beer CD. The feasibility and effect of deprescribing in older adults on mortality and health: a systematic review and meta-analysis. *Br J Clin Pharmacol* 2016; 82:583–623.
- [83] Saini P, Loke YK, Gamble C, Altman DG, Williamson PR, Kirkham JJ. Selective reporting bias of harm outcomes within studies: findings from a cohort of systematic reviews. *BMJ* 2014; 349:g6501.
- [84] Barnett K, Mercer SW, Norbury M, Watt G, Wyke S, Guthrie B. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012; 380:37–43.
- [85] Tooth L, Hockey R, Byles J, Dobson A. Weighted multimorbidity indexes predicted mortality, health service use, and health-related quality of life in older women. *J Clin Epidemiol* 2008; 61:151–159.
- [86] Williamson PR, Altman DG, Blazeby JM, Clarke M, Devane D, Gargon E, Tugwell P. Developing core outcome sets for clinical trials: issues to consider. *Trials* 2012; 13:132.

- [87] Idzerda L, Rader T, Tugwell P, Boers M. Can we decide which outcomes should be measured in every clinical trial? A scoping review of the existing conceptual frameworks and processes to develop core outcome sets. *J Rheumatol* 2014; 41:986–993.
- [88] Kirkham JJ, Gargon E, Clarke M, Williamson PR. Can a core outcome set improve the quality of systematic reviews?--a survey of the Co-ordinating Editors of Cochrane Review Groups. *Trials* 2013; 14:21.
- [89] Boers M, Kirwan JR, Wells G, Beaton D, Gossec L, d'Agostino M-A, Conaghan PG, Bingham CO, Brooks P, Landewé R, March L, Simon LS, et al. Developing core outcome measurement sets for clinical trials: OMERACT filter 2.0. *J Clin Epidemiol* 2014; 67:745–753.
- [90] MacLennan S, Bekema HJ, Williamson PR, Campbell MK, Stewart F, MacLennan SJ, N'Dow JM, Lam TB. A core outcome set for localised prostate cancer effectiveness trials: protocol for a systematic review of the literature and stakeholder involvement through interviews and a Delphi survey. *Trials* 2015; 16:76.

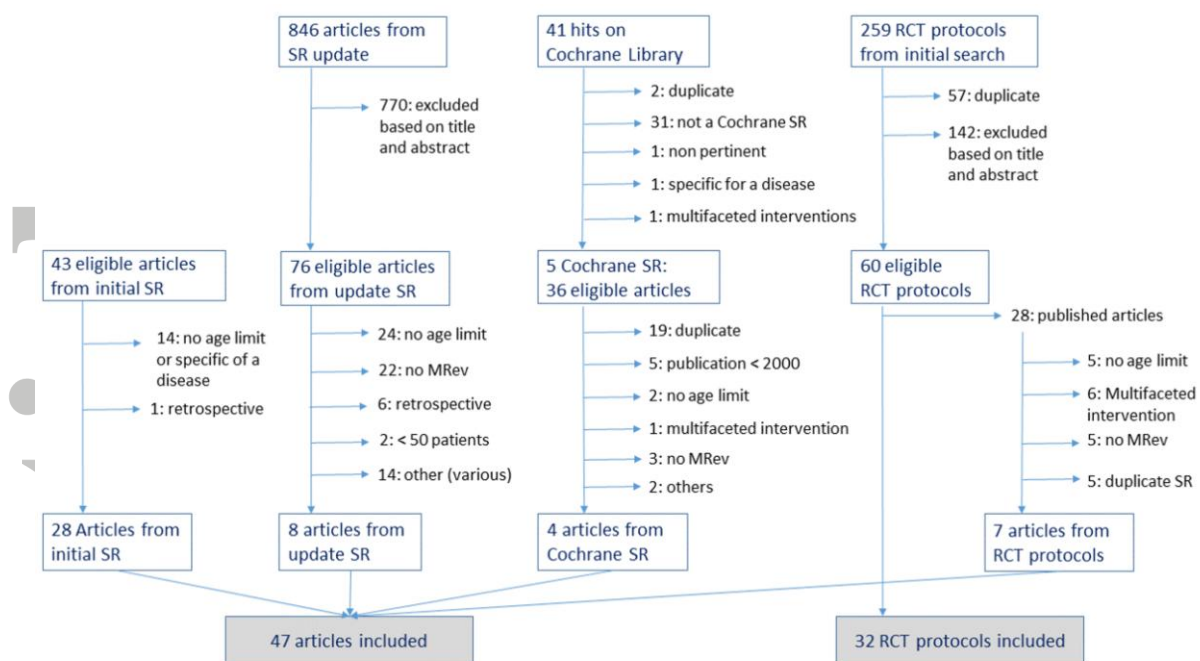


Figure 1: Flowchart of included studies and RCT protocols.

Abbreviations: RCT: Randomized controlled trials; MRev: Medication Review; SR: Systematic review

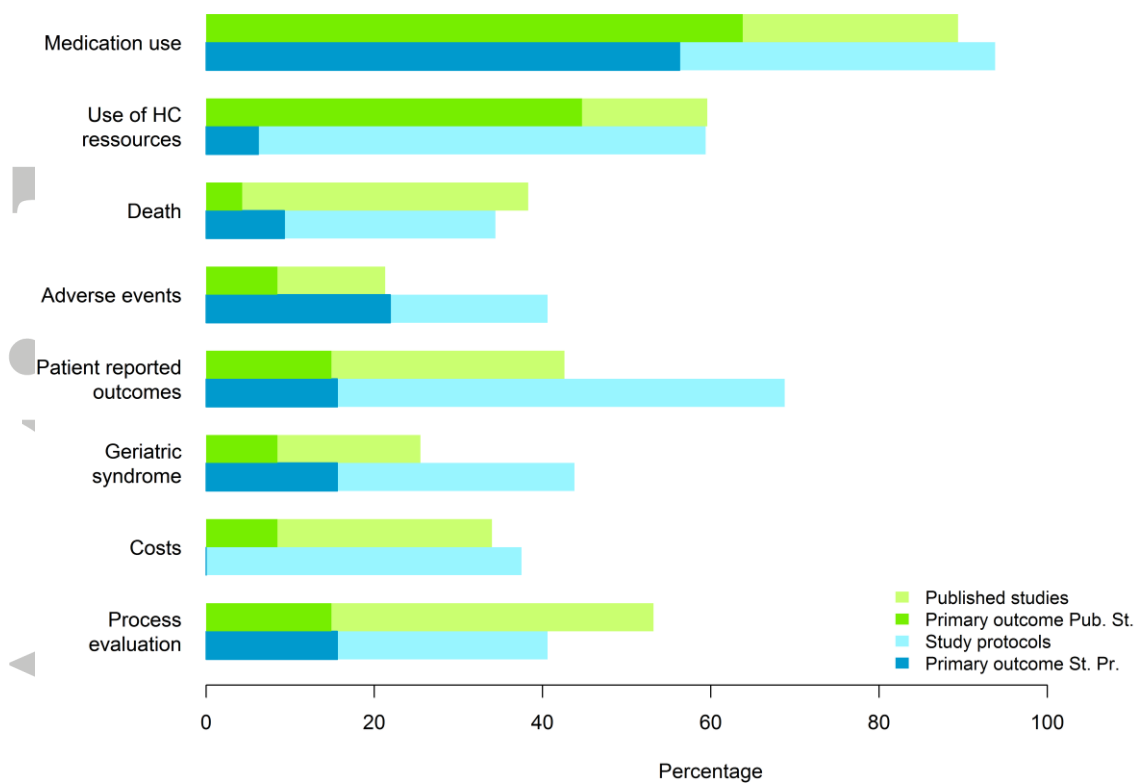


Figure 2: Percentage of health domains covered by the 47 published studies and 32 RCT protocols included in the systematic review, according to the outcomes identified. The percentage of studies in which the domain was covered by a primary outcome is given in darker colour.

Abbreviations: HC: healthcare; Pub. St.: published studies; St. Pr.: study protocols

For the full list of subdomains contained in each domain, please refer to eTable 1.

Table 1: Summary characteristics and demographics of included studies (published studies included 35 randomized controlled trials and 12 prospective studies).

	Published studies (n=47)	RCT protocols (n=32)
Number of study participants		
Median	334	300
Interquartile range	[170; 568]	[195; 600]
Range	[50; 7202]	[50; 3685]
Average age		
Median	80	
Interquartile range	[75.7; 82.7]	
Range	[73.5; 86.8]	
Setting		
Hospital	15 (32%)	11 (34%)
Community	19 (40%)	16 (50%)
Nursing homes	13 (28%)	5 (16%)
Country		
EU	28 (Belgium 2; Denmark 3; Germany 1; Ireland 3; The Netherlands 1; Spain 2; Sweden 5; UK = 11)	25 (Belgium 2; France 1; Germany 7; Ireland 2; Italy 1; Netherlands 6; Norway 1; Slovenia 1; Spain 1; Sweden 1; Europe MC 1)
Australia	8	3
USA	7	1
Others	4	3
Year of publication		
2000 – 2005	14 (30%)	
2006 – 2010	6 (13%)	
2011 – 2015	27 (57%)	
Number of outcomes		
Median	7	7
Interquartile range	[5; 10]	[6; 9]
Range	[1; 14]	[2; 19]

Table 2: Number of outcomes per health domain with the clarity of the measurement instrument used to measure them, as identified in the published studies or in RCT protocols.

	Outcomes				Measurement reproducible*			
	Published studies (317 outcomes)		RCT protocols (240 outcomes)		Published studies		RCT protocols	
	n	% ^(a)	n	% ^(a)	n	% ^(b)	N	% ^(b)
Medication use	99	31%	51	21%	64	65%	22	43%
Use of HC resources	70	22%	44	18%	43	61%	6	14%
Adverse events	11	3%	17	7%	8	73%	10	59%
Death	18	6%	11	5%	13	72%	2	18%
Patient reported outcomes	32	10%	38	16%	20	63%	31	82%
Geriatric syndrome	24	8%	42	18%	20	83%	29	69%
Costs	21	7%	16	7%	7	33%	4	25%
Process evaluation	42	13%	21	9%	22	52%	3	14%

Abbreviations: HC: healthcare

a) Based on the total number of identified outcomes (n = 317 for published studies; n = 240 for RCT protocols)

b) Based on the total number of outcomes identified in the given domain (value is “n” of the column “Outcomes”)

* The method of measurement was considered clearly defined if the reviewer believed that another author could reproduce the procedure and its measurement with the explanations given in the method section.

Appendix 1: Search strategy**Medication reconciliation****Embase (2000-2014)**

1. medication reconciliation.mp. or exp medication therapy management/
2. medication discrepancy.mp.
3. adverse drug event\$.mp.
4. 1 or 2 or 3
5. exp hospital/
6. exp patient admission/
7. exp patient discharge/
8. exp patient transfer/
9. exp emergency medicine/
10. exp emergency health service/
11. 5 or 6 or 7 or 8 or 9 or 10
12. 4 and 11
13. limit 12 to (english language and embase and yr="2000 - 2014")
14. exp general practice/
15. exp general practitioner/
16. exp primary health care/
17. 14 or 15 or 16
18. 4 and 17
19. limit 18 to (english language and embase and yr="2000 - 2014")
20. exp home for the aged/
21. exp nursing home/
22. exp elderly care/
23. residential aged care facilities.mp.
24. 20 or 21 or 22 or 23
25. 4 and 24
26. limit 25 to (english language and embase and yr="2000 - 2014")
27. 13 or 19 or 26

Ovid Medline (2000-2014)

1. medication reconciliation.mp. or exp medication therapy management/
2. medication discrepancy.mp.
3. adverse drug event\$.mp.
4. 1 or 2 or 3
5. exp hospital/
6. exp hospital admission/
7. exp hospital discharge/
8. patient transfer.mp.
9. exp emergency medicine/
10. exp emergency health service/
11. 5 or 6 or 7 or 8 or 9 or 10
12. 4 and 11
13. exp general practice/
14. exp general practitioner/
15. exp primary health care/
16. 13 or 14 or 15
17. 4 and 16
18. exp homes for the aged/
19. exp nursing homes/
20. exp health services for the aged/
21. exp elderly care/
22. residential aged care facilities.mp.
23. 18 or 19 or 20 or 21 or 22

24. 4 and 23
25. 4 or 12 or 24
26. limit 21 to (english language and yr="2000-2014")

PscInfo (2000-2014)

1. medication reconciliation.mp
2. medication discrepancy.mp.
3. adverse drug event\$.mp.
4. 1 or 2 or 3
5. exp hospitals/
6. exp hospital admission/
7. exp hospital discharge/
8. exp client transfer/
9. emergency medicine.mp.
10. exp emergency services/services/
11. emergency medical services.mp.
12. 5 or 6 or 7 or 8 or 9 or 10 or 11
13. 4 and 12
14. exp family physicians/
- 15 exp primary health care/ or exp family medicine/
16. exp general practitioners/ or exp general practice.mp
17. 14 or 15 or 16
18. 4 and 17
19. exp nursing homes/ or exp residential care institutions/ or exp elder care/
20. health services for the aged.mp.
21. residential aged care facilities.mp.
22. 19 or 20 or 21
23. 4 and 22
24. 13 or 18 or 23
25. limit 24 to (english language and yr="2000-2014")

CINAHL (Jan 2000- Jan 2014)

1. (MH "Medication Reconciliation")
2. "medication discrepancy"
3. (MH "Adverse Drug Event+")
4. S1 OR S2 OR S3
5. (MH "Hospitals, Urban") OR (MH "Hospitals, Community") OR (MH "Hospitals, Public+")
- OR (MH "Hospitals, Rural")
6. "hospital admission"
7. "hospital discharge"
8. "patient transfer"
9. (MH "Emergency Medicine")
10. (MH "Emergency Service")
11. (MH "Emergency Medical Services+")
12. S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11
13. S4 AND S12
14. (MH "Family Practice") OR (MH "Physicians, Family")
15. (MH "Primary Health Care")
16. (MH "Medical Practice")
17. S14 OR S15 OR S16
18. S4 AND S17
19. "home for the aged"
20. (MH "Nursing Homes")
21. (MH "Health Services for the Aged")
22. "elderly care"
23. "residential aged care facilities"

24. S19 OR S20 OR S21 OR S22 OR S23
25. S4 AND S24
26. S13 OR S18 OR S25 Limiters – Date published from: 20000101-20140331; English Language

Medication review

Embase (2000-2014)

1. drug utilization review.mp.
2. medication review.mp.
3. medication therapy management.mp.
4. medication history review.mp.
5. medical history review.mp.
6. exp hospital/
7. exp hospital admission/
8. exp hospital discharge/
9. patient transfer.mp.
10. exp emergency medicine/
11. exp emergency health service/
12. 6 or 7 or 8 or 9 or 10 or 11
13. exp general practice/
14. exp general practitioner/
15. exp primary health care/
16. 13 or 14 or 15
17. exp home for the aged/
18. exp nursing home/
19. exp elderly care/
20. residential aged care facilities.mp.
21. 17 or 18 or 19 or 20
22. 1 or 2 or 3 or 4 or 5
23. 12 and 22
24. 16 and 22
25. 21 and 22
26. 23 or 24 or 25
27. limit 26 to (english language and embase and yr="2000 - 2014")

Ovid Medline (2000-2014)

1. exp hospital/
2. exp emergency medicine/
3. exp emergency health service/
4. exp general practice/
5. exp general practitioner/
6. exp primary health care/
7. residential aged care facilities.mp.
8. exp patient admission/ or exp patient discharge/ or exp patient transfer/
9. exp Homes for the Aged/ or exp Nursing Homes/ or exp Health Services for the Aged/
10. elderly care.mp.
11. 1 or 2 or 3 or 8
12. 4 or 5 or 6
13. 7 or 9 or 10
14. exp "Drug Utilization Review"/
15. medication review.mp. or exp Medication Therapy Management/
16. medication history review.mp.
17. medical history review.mp.
18. 15 or 16 or 17
19. 11 and 18
20. 12 and 18

21. 13 and 18
22. 19 or 20 or 21
23. limit 22 to (english language and yr=2000 - 2014)

PsycInfo (2000-2014)

1. exp Hospitals/
2. exp Hospital Admission/
3. exp Hospital Discharge/
4. exp Client Transfer/
5. emergency medicine.mp.
6. exp Emergency Services/
7. emergency medical services.mp.
8. 1 or 2 or 3 or 4 or 5 or 6 or 7
9. exp Family Physicians/
10. exp Primary Health Care/ or exp Family Medicine/
11. exp General Practitioners/ or general practice.mp.
12. 9 or 10 or 11
13. exp Nursing Homes/ or exp Residential Care Institutions/ or exp Elder Care/
14. health services for the aged.mp.
15. residential aged care facilities.mp.
16. drug utilization review.mp.
17. medication review.mp.
18. medication therapy management.mp.
19. medication history review.mp.
20. medical history review.mp.
21. 16 or 17 or 18 or 19 or 20
22. 8 and 21
23. 12 and 21
24. 13 or 14 or 15
25. 21 and 24
26. 22 or 23 or 25
27. limit 26 to (english language and yr=2000 - 2014)

CINAHL (Jan 2000- Jan 2014)

1. (MH "Hospitals, Urban") OR (MH "Hospitals, Community") OR (MH "Hospitals, Public+") OR (MH "Hospitals, Rural")
2. "hospital admission"
3. "hospital discharge"
4. "patient transfer"
5. (MH "Emergency Medicine")
6. (MH "Emergency Service")
7. (MH "Emergency Medical Services+")
8. S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11
9. (MH "Family Practice") OR (MH "Physicians, Family")
10. (MH "Primary Health Care")
11. (MH "Medical Practice")
12. S9 OR S10 OR S11
13. "Home for the aged"
14. (MH "Nursing Homes")
15. (MH "Health Services for the Aged")
16. "Elderly care"
17. "Residential aged care facilities"
18. S13 OR S14 OR S15 OR S16 OR S17
19. (MH "Utilization review")
20. "Medication management therapy"
21. "Medical history review"

4

22. "medication history review"
23. S19 OR S20 OR S22
24. S8 AND S23
25. S8 AND S24
26. S18 AND S24
27. S24 OR S25 OR S26 Limiters – Date published from: 20000101-20140331; English Language